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Authors' reply

Matthias Maiwald and Andreas Widmer express concern with the WHO recommendation on surgical site preparation.[1,2] WHO guidelines are developed using processes and methods to ensure robust recommendations.[3] Specifically, this recommendation was informed by a systematic review and several meta-analyses, including one of six randomised controlled trials comparing alcohol-based chlorhexidine with povidone-iodine-alcohol (PVP-I) preparations that showed a greater reduction in surgical site infections (SSIs) with chlorhexidine (odds ratio [OR] 0·58, 95% CI 0·42–0·80).[1,2,4] We acknowledge that the study by Ngai and colleagues[5] was erroneously not included. However, when added to the WHO meta-analysis, the combined OR is similar (0·65, 95% CI 0·47–0·91). The study by Ostrander and colleagues[6] included in the analysis of Maiwald and Widmer was excluded from the WHO meta-analysis because it was not a randomised controlled trial.

Maiwald and Widmer excluded four studies because "inadequate or unknown antiseptics" were used. Three of them met prespecified WHO review inclusion criteria.[4] The exclusion of Cheng and colleagues[7] does not affect the results because no SSIs were recorded (appendix). Alcohol concentrations were unknown for the studies by Berry and colleagues[8] and Veiga and colleagues,[9] but there is no reason to believe that concentrations were inadequate. Of note, Maiwald and Widmer incorrectly claim that the trial by Berry and colleagues was outside the time limits of our review, which covered the period Jan 1, 1960, to Aug 15, 2014.[4] Finally, Maiwald and Widmer excluded the trial by Salama and colleagues,[10] but appropriate concentrations were reported in this manuscript (70% alcohol combined with either 2% chlorhexidine or PVP-I). When this study is added to the Maiwald and Widmer meta-analysis, the results change substantially, showing that chlorhexidine is superior to PVP-I (risk ratio [RR] 0·77; 95% CI 0·63–0·94). When updating the WHO analysis with the recent trial by Broach and colleagues,[11] chlorhexidine continues to be superior (OR 0·73, 95% CI 0·55–0·97). The Salama trial was not included in the WHO systematic review as it was not indexed in PubMed or other databases. However, when adding it to the updated analysis, the OR becomes 0·65 (95% CI 0·47–0·91; appendix).

In conclusion, the results of the updated meta-analysis that informed the WHO recommendation remain unchanged, with improved quality of evidence, due to higher precision. Although not statistically significant, the results reported by Maiwald and Widmer also favour chlorhexidine. We emphasise that post-hoc exclusions of trials from systematic reviews and meta-analyses are problematic and likely to introduce bias.[12] This recommendation is central to SSI prevention, but the WHO guidelines recognised that the availability of chlorhexidine-alcohol-based preparations remains limited and can be an additional cost in developing countries. However, local production is possible and should be encouraged.[1,2,13] We are confident that similar to the widespread adoption of alcohol-based hand rubs, a change in practices is possible, and will benefit patients.

We declare no competing interests.

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